REMARKS

Claims 1-21 are pending in the instant application. Claims 1-13 have been rejected by the Examiner. Claims 14-21 have been withdrawn from consideration by the Examiner.

By the above amendments Claims 1-10 have been amended to more particularly point out and distinctly claim the subject matter, which Applicants regard as the invention. More specifically, the claims have been amended to comply with the restriction requirement and election of invention.

Applicants respectfully acknowledge and thank the Examiner for discussing the application with the applicants' attorney, Hal Brent Woodrow and applicants' agent, Maria Shchuka on November 4, 2004. As discussed in that telephone conversation, the R^1 and R^2 groups have been amended to remove hetero-ring containing groups. However, the current amendment does not remove the "heteroaryl" and "aryl substituted heteroarylaminosulfonyl" substituents (see for example, Claim 1, page 4, line 18), which are optional substituents on the R^1 and / or R^2 groups. Thus, for example, an R^1 or R^2 group such as C_{1-4}alkyl optionally substituted with a heteroaryl group (as in Compound #282 on page 70) or an aryl group optionally substituted with an aryl substituted heteroarylaminosulfonyl (as in Compound #283 on page 82) would not be removed by the current amendment. The Examiner has agreed to review the completed search to determine if the search was adequate to cover said substituents on the R^1 and / or R^2 groups and advise Applicants accordingly.

Applicants submit that the amendments are fully supported by the specification as filed, and no new matter is being added. After entry of the amendments, Claims 1-13 will remain pending and under consideration.

Reconsideration of the captioned application based on the previous amendments and following remarks is respectfully requested.

The Examiner asserts that the instant application contains claims directed to patentably distinct species of the claimed invention and has required Applicants to elect a single disclosed species under 35 U.S.C. §121.

In the Office Action, restriction was required in the above-referenced application to one of the following groups:

Group I. Claims 1-13 in part, drawn to compounds and pharmaceutical compositions wherein R3 is an aryl, X is NR1R2, R1 and R2 are non-hetero ring containing And the circle is a naphthyl, phenyl or acenaphthyl;

Group II. Claims 1-13 in part, drawn to compounds, pharmaceutical compositions, wherein R3, R0 and the circle are other than in group I;

Group III. Claims 14-19, drawn to various methods of treating diseases;

Group IV. Claims 20, 21 in part, drawn to compounds of formula E, R3 is an aryl, Y is L'n is a circle and the circle is an aryl;

Group V. Claims 20 and 21 in part, drawn to compounds wherein R3, Y and the circle are other than in group IV;

Applicants hereby affirm the provisional election of the invention of Group I, and the further election of the species disclosed as Compound # 438 on page 74, the election having been made during the telephone conversation with the Examiner on July 08, 2004.

This election of species is without traverse to the extent that it is understood that (a) the requirement will be withdrawn upon the finding of an allowable genus; and (b) any species withdrawn from consideration will be transferred to the elected subject matter unless it is found patentably distinct from the elected or allowed claims.

There are two criteria for a proper restriction requirement between patentably distinct inventions: (1) the inventions must independent or distinct as claimed; and (2)

there must be a serious burden on the Examiner if restriction is not required. MPEP 803. Applicants agree with the Examiner's findings that the alleged separate inventions are patentable over each other; however, Applicants urge that there is no serious burden on the Examiner in combining the restricted groups into one application. Therefore, Applicants respectfully request that the Examiner withdraw the restriction requirement.

Claims 14-21 have been maintained in the application to allow the rejoining of the method limited of the same scope as the elected compound claims, if the compound claims are found allowable.

Claims 1-13 have been rejected under 35 USC 112, first paragraph. The Examiner states that "the specification, while being enabling for thiophene as a het group and substituent, does not reasonably provide enablement for any and all the different hetergroup at the numerous and various positions."

Applicants respectfully traverse the rejection. Applicants submit that the specification adequately teaches one of ordinary skill in the art how to make the claimed compounds. More specifically, the specification, in Schemes 1-14 teaches how to make the compounds of the present invention, including how to make intermediates in the synthesis of the compounds of the present invention. Applicants maintain that the schemes as disclosed are not dependent on the heteroaryl or heterocycloalkyl group that is part of a substituent group and that one skilled in the art would be able to make the compounds of the present invention commensurate with the scope of the claims.

With respect to the adequacy of disclosure that a claimed genus possess an asserted utility (i.e. enablement of how to use the claimed compounds), the disclosure of representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if it would be deemed likely by one skilled in the art that the claimed genus would possess the asserted utility. The specification clearly discloses use of the

instant compounds for the treatment of ORL-1 receptor mediated disorders (*see, e.g.*, page 10, lines 1-21; page 44, lines 2-8; and page beginning on page 181 in Examples 67-74). Moreover, page 45, line 2-12 and page 114, line 1 through page 118, line 15 of the specification teaches how the compounds may be used (e.g., route of administration, dosages) to treat such disorders. Thus, Applicants urge that the instant specification provides a teaching of how to use the invention which would be credible to the skilled artisan, and moreover, that one of ordinary skill in the art would be able to use the compounds for the stated utility without undue experimentation.

Moreover, an Applicant's assertion of utility creates a presumption of utility and the Examiner has the initial burden of challenging a presumptively correct assertion of utility in the disclosure; only after the Examiner provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility. Applicants maintain that the Examiner has not provided evidence that would cause the skilled artisan to doubt Applicants' teachings of utility which are set forth in detail above. Therefore, Applicants maintain that the Examiner has failed to establish a *prima facie* case that the claimed invention lacks utility. (See *in re Marzocchi and Horton*, 439 F.2d 220, 169 U.S.P.Q. 367 (C.C.P.A. 971))

Applicants therefore respectfully request that the Examiner remove the rejection of Claims 1-13 under 35 U.S.C. 112, first paragraph.

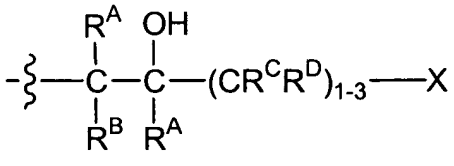
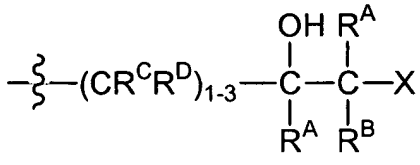
Claims 1-13 have been rejected under 35 U.S.C. 103(a) as allegedly unpatentable over US 4,329,353 Strokbroekx et al; US 6,043,366 Adams et al; US6,277,991 Hohlweg et al.; US 3,839,340 Scharpf; WO 99/59997 Watson Brett and also EP 0997464 A1 Ito Fumitaka et al.

More specifically, the Examiner alleges that "The only difference is that the R0 has an =O instead of a hydroxide... A ketone and a hydroxide are tautomers of each other and hence it would have been obvious for one skill in the art to make the hydroxy compound."

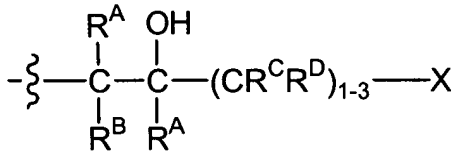
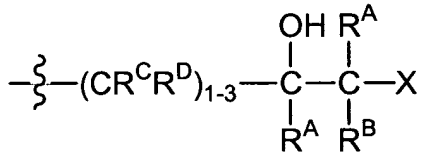
Applicants respectfully traverse the rejection. Applicants submit that a ketone and a hydroxide are not tautomers. Rather as shown in the theoretical scheme below,

a ketone will tautomerize to the corresponding enol – liberating an alpha hydrogen and resulting in the formation of a double bond between the carbon atom bound to the oxygen and an adjacent atom. (In order to convert a ketone to the corresponding hydroxide, the ketone must be oxidized, requiring a chemical reaction.) As such, Applicants submit that the tautomer of the prior art compounds would not fall within the scope of the compounds of the present invention, as the compounds of the present invention do not permit the presence of a double bond at the carbon substituted with the hydroxy group.

The Examiner further states "Also the chain may have no alkyl chain". Applicants interpret this statement as referring to the R^0 substituent on the compounds of the present invention and respond as below. As agreed in the telephone conversation with the Examiner on November 4, 2004, if this interpretation of the Examiner's statement is incorrect, Applicants respectfully request clarification to enable the applicants to fully respond to this rejection.

Applicants respectfully note that in the compounds of the present invention R^0 is selected from the group consisting of  and  . Therefore, there must exist <u>at least one carbon atom</u> between the 1,3,8-triazaspiro[4.5]decan-4-one core and the carbon atom substituted with the hydroxy group; <u>and at least one carbon atom</u> between the carbon atom

substituted with the hydroxy group and the X substituent. Applicants submit that the prior art references do not teach or suggest such a carbon spacer.

Finally, the Examiner alleges that "EP0997464 teaches the OH substituent on the alkyl group." Applicants maintain that the teaching of Fumitaka et al., in EP 0997464 would not motivate one skilled in the art to make the compounds of the present invention. Applicants respectfully refer the Examiner to the Federal Circuit Decision *In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550, 1552 (Fed. Cir. 1994), and maintain that the disclosure in Fumitaka et al., does not provide any teaching or suggestion for selecting the specific combination of substituents required to yield the R^0 substituents on the compounds of the present invention. Applicants further submit that Fumitaka et al., in EP 0997464 does not exemplify any compounds wherein the nitrogen at the 3-position of the 1,3,8-triazaspiro[4.5]decan-4-one is substituted with an alkyl chain which is further substituted with a hydroxy and a terminal amine group, a substituent group which would correspond to the R^0 substituent of the present invention (The compounds of the present invention define R^0 as is selected from  or ). Thus, Applicants maintain that Fumitaka et al., EP 0997464 as a whole would not apprise the ordinary artisan of the significance of the hydroxy-alkyl- portion of the R^0 substituent and thus would not render obvious the compounds of the present invention.

Applicants maintain that the prior art does not teach or suggest the compounds of the instant application and that one skilled in the art would not be motivated to make the compounds of the present invention. Applicants therefore respectfully request that rejection of Claims 1-13 under 35 U.S.C. 103(a) be withdrawn.

In view of the above remarks, Applicants maintain that the application is in condition for allowance and passage to issue is earnestly requested.

Respectfully submitted,

Hal Brent Woodrow

Hal Brent Woodrow
Attorney for Applicants
Reg. No. 32,501

Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, NJ 08933-7003
(732) 524-2976
Dated: November 15, 2004